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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,170	02/01/2002	Tse Wai-Choi Eric	109312.	9703

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EXAMINER	
GABEL, GAILENE	
ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 11/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/936,170	ERIC ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-18* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/18/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 25, 2006 has been entered.

Amendment Entry

2. Applicant's amendment and response filed September 25, 2006, is acknowledged and has been entered. Claim 1 has been amended. Claim 18 remains withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Currently, claims 1-18 are pending. Claims 1-17 are under examination.

Withdrawn Rejections

3. All rejections and objections not reiterated herein, have been withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, step a) is vague and indefinite in reciting, "wherein an unknown immunoglobulin is associated with the first molecule" because it is unclear how the unknown immunoglobulin is caused to be associated to the first molecule.

Claim 1, step a) is ambiguous and appears to be incomplete in reciting, 1) "wherein specific interaction of the first and second molecule leads to the generation of a signal", 2) "wherein an unknown immunoglobulin is associated with the first molecule", and 3) "wherein an intracellular target is associated with the second molecule" because it fails to recite positive and active method steps that define the claimed invention. It is specifically unclear what active method step is encompassed so as to cause specific interaction between the first molecule and the second molecule; what specific active method step is encompassed so as to associate an unknown immunoglobulin with the first molecule; and what specific active method step is encompassed so as to associate the intracellular target with the second molecule. Step a) only recites, "providing in an intracellular environment, a first molecule and a second molecule."

Claim 1, step b) is also vague and indefinite in reciting, "assessing" because the term "assess" is a subjective term that lacks a comparative basis for defining its metes and bounds. How is intracellular binding "assessed?" Perhaps, Applicant intends

"determining the intracellular binding" (so as to be consistent with the preamble)... by detecting for or monitoring the signal.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

In this case, the specification does not appear to provide any literal or descriptive support for the recitation of "unknown immunoglobulins" as recited in the context of the claimed method. Applicant points to several parts of the specification for support of the recitation, "specific interaction" wherein adequate support and description of such phrase is warranted; however, the recitation of "unknown" that delimits the scope of population of immunoglobulins used in the claimed method, is not literally supported or adequately described. Applicant points to page 28, lines 29-33 which provides that the invention "permits the screening of entire antibody libraries such as phage libraries, without prior application of phage display to isolate the antibodies which bind to the desired antigen"; however, it fails to provide literal support for the recitation of only

"unknown" antibodies used in the method for determining binding interaction. Furthermore, none of the originally filed claims recited the limitation in question. Recitation of claim limitation lacking literal or adequate descriptive support in the specification or originally filed claims constitutes new matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Gargano et al. (From Phage Libraries to Intracellular Immunization, Intracellular Antibodies: Development and Applications (1997) Chapter 10, pages 174-186)).

Gargano et al. teach determining efficient binding between intracellular immunoglobulins (scFv) expressed in a yeast two hybrid format and corresponding target antigens in an intracellular environment (yeast cells), and isolating immunoglobulins which bind successfully (see page 176, second full paragraph, and Figure 10.1). Gargano et al. provide an interaction trap (two hybrid system) having a first molecule and a second molecule in a modular domain structure as in eukaryotic transcription factors: transcriptional activation domain and a DNA-binding domain, which exist as separable domains, but associate to form an active reporter molecule

(construct). Activation of the reporter construct occurs when the two domains, expressed as activation domain (VP16) and DNA-binding domain (LexA) fusion proteins, are brought together through binding interaction of two polypeptides that are associated (fused) thereto in an assay, leading to generation of a signal that can be monitored by change in optical property (colorimetric assay). The two polypeptides are an scFv fragment and a target antigen associated (fused) to each of the VP16 activation domain and LexA DNA-binding domain, respectively. According to Gargano et al., the level of reporter activation correlates well with specific binding of proteins which further gives an indication of the strength of the interaction (see page 174, fourth full paragraph to page 176, first full paragraph). The active reporter molecule may be an enzyme and the method is performed in the presence of a substrate (see page 177, first full paragraph and Figure 10.1 (D)). The immunoglobulins are provided by immunoglobulin-encoding nucleic acids within mammalian cells, from phage libraries encoding a repertoire of immunoglobulins (see page 177, second to fourth full paragraphs). The libraries can be constructed from nucleic acids isolated from an organism which has been challenged by antigen (see page 180, first and second full paragraph). Gargano et al. teach selecting immunoglobulins and further subjecting them to functional intracellular assay (see Figure 10.2). Cells can be sorted (rescued) on the basis of phenotype conferred by the intracellular immunoglobulins.

Response to Arguments

7. Applicant's arguments filed on September 25, 2006 have been fully considered but they are not persuasive.

A) Applicant argues that the claims are not anticipated by Gargano et al. because Gargano does not teach that the immunoglobulin associated with the first molecule is unknown and is screened against a desired antigen or target, as described in Applicant's specification at page 28, lines 29-33. Applicant specifically contends that Gargano et al. is merely precatory and fails to teach an actual direct screen or selection of several unknown immunoglobulins against a given antigen.

Upon further consideration, the Gargano reference appears to anticipate the claimed invention because the teaching and suggestion provided at page 176, second full paragraph and page 174, second full paragraph, read on the claimed invention which recites that the immunoglobulins are unknown. In page 176, second full paragraph, Gargano literally and specifically provides, "The initial proof of antigen-antibody interaction in the two hybrid format, using known antigen-antibody pair, is presently being extended to the analysis in the two hybrid system of small polyclonal repertoires selected from phage display libraries by panning against a given antigen. In this format, the experimental design is tailored for the selection (i.e. screening) of a polyclonal population of affinity purified ScFv fragments on the basis of their binding to a given antigen, regardless of functional consequences." Further in page 174, second full paragraph, Applicant literally and specifically provides "... downstream use as intracellular antibodies. This relates to the fact that only by exploiting the phage display technology, it is possible to have at our disposal recombinant polyclonal repertoires of

antigen binding antibodies. This possibility lays the ground for new selection schemes whereby intracellular expression and targeting can be exploited: - to select antibodies on the basis of binding to a given antigen under conditions of intracellular expression (binding selection); - to select (i.e. screen for) antibodies on the basis of given function or phenotype provided by the intracellularly expressed antibodies. Engineering these repertoires into a format suitable for intracellular expression in eukaryotic cells, and applying appropriate selective pressures, should allow us to isolate new antibody specificities previously unknown, on the basis of the conferred phenotype." Accordingly, it is deemed that Gargano anticipates the claimed invention because Applicant's opinion of Gargano's teaching as merely precatory in regards to application of the claimed method of screening or selection from unknown immunoglobulins, is not warranted.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., selecting or screening unknown immunoglobulins [associated with the first molecule] against a known antigen) are not recited in the rejected claims. Specifically, there are no method steps that encompass or recite a screening or selection procedure. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

8. For reasons aforementioned, no claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gailene R. Gabel
Patent Examiner
Art Unit 1641
October 18, 2006